THE DAWN OF THE CELL THEORY

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HOW often it happens that a great discovery, before it finally flashes out upon the world, smoulders for a long time in men's minds, dimly understood, its full significance unfelt! So it was with wireless telegraphy, which by Marconi's great imagination and skill was transformed from a piece of laboratory apparatus, capable of transmitting electric waves across a room, into a great system, flashing messages across oceans and around the world. So it was with each of the three great biological discoveries of the nineteenth century, the cell theory, organic evolution and Mendelism. The last, indeed, as the reader knows, lay dormant during the final third of the century, ready to spring into rapid and luxuriant growth at the opening of the twentieth.

Organic evolution, it is well known, had its birth in the master mind of the great French naturalist, Lamarck, at the very beginning of the nineteenth century, fifty years before the appearance of Darwin's "Origin of Species," but probably few, even among the ranks of professional biologists, are aware that the cell theory owes its conception to the same fertile, comprehensive mind.

Probably no statement in the history of biology is more widely accepted and quoted by biologists today than that the cell-theory, *viz.*, that all plants and animals, as well as their embryonic forms, are composed of similar elementary parts, the cells, founded in 1838 and 1839 by the German botanist Schleiden and his friend, Schwann. So when the present writer first read in Lamarck's "Philosophie Zoologique," published in Paris in 1809, the following statement, he could hardly believe his eyes. "No body can possess life if its containing parts are not a *cellular tissue*,[1] or formed by cellular tissue." And further, "Thus every living body is essentially a *mass of cellular tissue* in which more or less complex fluids move more or less rapidly; so that, if this body is very simple, that is, without special organs, it appears homogeneous, and presents nothing but *cellular tissue* containing fluids which move within it slowly; but, if its organization is complex, all its organs

[1] The italics in this translation correspond to those in the original.

without exception, as well as their most minute parts, are enveloped in cellular tissue, and even are essentially formed of it."

In the introduction to the chapter on the "Physical Causes of Life," in which the words just quoted occur, Lamarck calls attention to the phenomena of organization and its development, especially in the lower animals, the consideration of which should convince the reader, he says, that (1) "The entire operation of nature in forming her direct creations [the development of the individual] consists in organizing into *cellular tissue* the little masses of gelatinous or mucilaginous matter that she finds at her disposal and under favorable circumstances; in filling these cellular masses with fluids that they are adapted to contain; in vitalizing them by setting the contained liquids in motion with the aid of subtle exciting fluids that ceaselessly flow into them from the surrounding medium."

How much more modern this sounds than the idea that those of us who are biologists at the beginning of the twentieth century are accustomed to hold regarding the doctrine of those who worked and wrote at the beginning of the nineteenth! We have been wont to think of the conception of the cell in those earlier days as being a cavity surrounded by a cell-wall that was then regarded as all-important, and here we find Lamarck declaring that the "little masses of gelatinous or mucilaginous matter," the protoplasm of later writers, organized into cellular tissue, are the essential vital elements, just as we hold to-day! Of the "subtle exciting fluids that ceaselessly flow into them from the surrounding medium," we are even to-day almost in ignorance. What Lamarck had in mind, as one gathers from reading elsewhere in the same work, was electric action. Lamarck seems to have anticipated by more than a hundred years the application of the electron theory to the cell, a field which to-day is still almost wholly unexplored.

Lamarck's conception of the mechanics of development set forth in his second essential condition of life is as follows:

> *Cellular tissue* is the matrix (literally "gangue," or vein-stone) in which all organization has been established, and through the medium of which the different organs have been successively developed by the movement of the contained fluids, which have gradually modified this cellular tissue.

The comparison of cellular tissue to a matrix or veinstone, in which the fluid living substance, energized and set in motion by forces acting chiefly from without, is gradually moulded into definite organs is not an apt simile, to be sure, from our present point of view, and yet even to-day are we able to replace it by a metaphor that would be more exact? In the conception now in vogue, however, the shaping of organs is attributed especially to the enzyme-

like action of the chromosomes, to *internal* physico-chemical phenomena which Lamarck covered under the expression movements of "fluides contenables," acted upon by subtle exciting fluids, "which ceaselessly flow in from the surrounding media." Present conceptions (Weismannism and Mendelism) lay great emphasis upon the rôle in development believed to be played by cell nuclei, which were unknown to Lamarck. Thirty years later, when Schleiden and Schwann approached the subject, cell-nuclei had been discovered.

It is worth a passing notice that in a clear and keen analysis of the differences between organic and inorganic bodies, which Lamarck states had been already discussed by M. Richerand, but to which he adds his own ideas, growth of organisms is described as being by "intus-susception," a notion that the present writer has been accustomed to regard as much more modern.

The statements thus far mentioned were taken from the first volume of the "Philosophie Zoologique." In the second, Lamarck devotes an entire chapter to cellular tissue, in which he says: "It has been recognized for a long time that the membranes that form the envelopes of the brain, of nerves, of vessels of all kinds, of glands, of viscera, of muscles and their fibers, and even the skin of the body, are in general, the productions of *cellular tissue*. However, it does not appear that any one has seen in this multitude of harmonizing facts anything but the facts themselves; and no one so far as I know, has yet perceived that *cellular tissue* is the general matrix of all organization, and that without this tissue no living body would be able to exist nor could have been formed. In a foot-note he adds, "Since the year 1796 I have been accustomed to set forth these principles in the first lessons of my course."

In the same year (1809) that Lamarck published this classic work, another great Frenchman, Mirbel, brought out the second edition of his "Exposition de la Théorie de l'Organisation Végétale." The general conclusion reached in the book was that "The plant is wholly formed of a continuous cellular membranous tissue," or stated as the first of a set of botanical "aphorisms" that he had prepared for the Musée de l'Histoire Naturelle to accompany a large and beautiful plate illustrating the finer structure of plants, "Plants are made up of cells, all parts of which are in continuity and form one and the same membranous tissue."

Mirbel was probably the most distinguished and industrious plant anatomist at the opening of the nineteenth century, and it is interesting to trace in his works the earliest stages of the development of the cell theory. In 1802 appeared his "Traité d' Anatomie et de Physiologie Végétales." Here are only the incoherent ele-

ments of a cell theory. He had not yet arrived at the idea that all plants are essentially cellular, and he regarded the cell-wall as of primary importance. Cells he found, in fungi and Fucus, in the epidermis and parenchyma of the higher plants, more abundantly in herbs than in trees, in sprouts than in old wood. The embryo was composed ''almost entirely'' of cell tissue. But he had not at the time discovered the origin of the *tubes* that are embedded in the deeper tissues of plants, so that this earliest version of the first ''Aphorism,'' quoted above, then read: ''Plants appear to be entirely composed of cells and of tubes, all parts of which are continuous.'' Tubes, however, it will be noted, were omitted from this aphorism when it appeared in 1809.[2]

How much collaboration there may have been between Lamarck and Mirbel, who was thirty-two years his junior, does not appear from evidence now at hand, except that both must have been closely associated in the Musée de l'Histoire Naturelle, but in 1809 both entertained somewhat similar views regarding the structure of plants.

As Mirbel expressed it in his letter to Treviranus included in his ''Théorie de l'Organisation végétale,'' all plants are formed of ''one and the same membranous tissue, variously modified,'' not of distinct and separate elementary organs existing independently and held together by interwoven tubes and fibers; moreover he laid great stress upon his observation that cells freely communicate with one another by pores.

Whether Lamarck based his more extensive generalizations, which included animals as well as plants, upon Mirbel's observations as well as upon his own, it is evident that both held in 1809 the essential features of the cell theory.

As Mirbel's first aphorism stated it, ''Les végétaux sont composés de cellules, dont toutes les parties sont continues entre elles, et ne présentent qu'un seul et même tissu membraneux.''

It must be recognized, however, that Mirbel laid emphasis upon the membranous cellular tissue as fundamental, rather than upon the cell as a unit. The folding and modification of this tissue during development resulted in the specialized full-grown plant. And, to Lamarck, cellular tissue was the matrix within which the organs, *i. e.*, the blood vessels, nerves, and other ''tubes'' are moulded by the movements of the contained fluids. The thought of both was centered upon the organism as a whole and

[2] It was not until 1832-33 that his studies on the structure of Marchantia convinced him by direct observation that the tracheæ are formed from cells, and do not constitute an exception to the rule that all plant structures are cellular in origin.

the primacy of cellular tissue. But to Mirbel's mind this tissue was membranous. Bichat had just laid the foundations of animal histology by the classification and description of tissues among which he included membranous cellular tissue, by which he apparently meant undifferentiated connective tissue. Probably this important and remarkable work influenced Mirbel. Neither Mirbel nor Lamarck apparently thought of the individual cell as the elementary unit.

The idea of the individuality of the cell, an important contribution to the cell theory, is due to Dutrochet, 1824, who set the notion forth in a book apparently very little known at present.

This is a fascinating account of his own physiological experiments on the movements of the sensitive plant, on growth movements and heliotropism in plants, and on muscular action in animals. He was also something of a histologist, though his microscopes (simple lenses of high magnification) were undoubtedly poor, and his methods of treating tissues with nitric acid and strong alkalis a bit drastic. After summarizing the then recent (1824) researches of Milne Edwards (Mémoire sur la structure élémentaire des principaux tissus organiques), who had found in the tissues of animals nothing but masses of globules (globules agglomérés) he says, "I have verified the exactness of these observations: everywhere, indeed there is found in the organs of animals only globular corpuscles, sometimes united into longitudinal and linear series, sometimes massed in a confused manner." After numerous details, which we pass over, he states, "From this we may draw the general conclusion that the globular corpuscles, which by their assemblage make up all the organic tissues of animals, are actually globular cells of exceeding smallness, which appear to be united only by a simple adhesive force; thus, all tissues, all animal organs, are actually only a cellular tissue variously modified. This uniformity of finer structure proves that organs actually differ among themselves merely in the nature of the substances contained in the vesicular cells, of which they are entirely composed."

Then, after telling of the wonderful diversity of cell organization in plants, which he believed to be greater than in animals, he exclaims, "One can not conceive how a diversity of products so astonishing can be the work of a single organ, of the cell! This astounding organ, in the comparison that can be made between its extreme simplicity and the extreme diversity of its real nature, is truly the fundamental element (pièce fondamentale) of organization; everything, indeed, in the organic tissue of plants, is evidently derived from the cell, and observation has just proved to us that

it is the same with animals.'' Thereupon he points out that the blood itself is a fluid tissue, capable by coagulation of becoming like other tissues. In it the corpuscles, which he regards as cells, float freely.

But closer examination of Dutrochet's work reveals the fact that the cell theory which he held rested upon an insecure basis of fact. This was due not so much to imperfect observation with imperfect microscopes as to the fact that the ultimate organic unit had not yet been accurately defined. That every bit of living matter has its spherical nucleus was still undiscovered.

It was the aim of the naturalists of that period, however, to resolve all organisms into their ultimate parts. The ultimate parts that they found were minute globules of various sizes, some cells, some nuclei, some nucleoli, some merely granules within the cytoplasm. It was unfortunately upon the observation of these diverse globules that Dutrochet based his excellent conclusions. He undoubtedly saw cells, and his figure of a segment of an arm of Hydra seems to prove that he saw nuclei, but the latter were to him ''nervous corpuscles,'' corresponding to bodies in the cells of the sensitive plant, which, his figures suggest were probably nucleoli or chromosomes. He showed corresponding granules also in the stem of Vorticella, arranged in linear order. Possibly these were cytoplasmic microsomes; certainly they were not cells.

The fundamental ideas of Schleiden and Schwann's cell theory were thus contained in the writing of these and other writers of the previous generation, who have not been recognized as its founders chiefly because the term cell, in their minds, was loosely defined. They had not learned that a typical unit mass of living matter has a single spherical nucleus. The discovery of this fact made the establishment of the cell theory sure, and in the present writer's opinion was even more important than the work of Schleiden.

Although the nucleus had been seen and figured by still earlier writers, its general occurrence in plant cells was first recognized by Robert Brown, 1833, a by-product of his work on fertilization in orchids and milkweeds.[3]

It was this work that furnished Schleiden with his inspiration, and led to his attempt to discover the relation of the nucleus to the development of the cell, to answer the question: ''How does this peculiar little organism, the cell, originate?'' This question he answered to his own satisfaction, though not to ours, when he described the birth of the young cell by the appearance of a sort

[3] p. 710-713. See *References to Literature.*

of lens-shaped bud upon the surface of the nucleus, or "cytoblast," as he renamed it.

It is difficult in these days to follow Schleiden through the details of his "discovery," but it would appear that by the great solubility of cellular tissue (cell walls), when not too thick, a fact which "some physiologists ——— have felt prepared to deny," the new-born cells first float free, then become massed together and secrete about themselves new walls, in which the nucleus becomes imbedded, if it has not already been absorbed or "cast off as a useless member." This incorrect idea of the general method of formation of new cells overemphasized their freedom, and is reflected in Schleiden's oft-quoted remark of that "Each cell leads a double life: an independent one, pertaining to its own development alone; and another incidental, in so far as it has become an integral part of the plant." It is around this version of the cell theory, further elaborated by Haeckel in his conception of the organism as a cell state or cooperative colony of free citizens, that much discussion and criticism of the cell theory has centered, led particularly in the last decade of the nineteenth century by Sedgwick, 1895, and Bourne, 1896. The outcome of this and still more recent discussions has been to swing the emphasis away from Schleiden's version, founded as it was upon misconceptions of the process of the formation of new cells and ignorance of the universal fact of nuclear and cytoplasmic division, back to the point of view of Lamarck and Mirbel that, in its growth, the cellular organism reacts as a whole.

Although Schleiden did not originate the idea of the cell theory, which, as his "Phytogenesis" shows, he got directly from Mirbel and his own German contemporary, Meyen, he did good service to science by calling attention to Robert Brown's discovery of the universal occurrence of the nucleus in plant cells, and especially by stimulating his friend Schwann in the prosecution of those important and epoch-making studies into the structure of animal cells that we have so long regarded as the foundation of the cell theory.

Schwann, as the preface of his classic work indicates, evidently knew little of the ideas of the French biologists who had drawn the plans and begun to lay the foundations of the cell theory thirty years earlier. The physiologist, Dutrochet, for example (whom Schwann does not mention), while he had held the Lamarck-Mirbel cell theory, having no standard by which to decide what a cell is, had left the notion of the animal cell in that confused, almost chaotic state, in which Schwann says that he found it. Schwann does refer to an isolated observation of Turpin, who compares the

cells of the epithelium of the vagina with those of the parenchyma of plants, and of Dumortier, who had drawn the conclusion, from researches into the embryology of the snail, that Mirbel's proof of the development of plants from a single cellular tissue would not apply to animals, but there is probably little doubt that Schwann found in contemporary literature much confusion regarding the cell in animals.

The beautiful plates which Schwann has left us are a perennial memorial to his skill as an investigator and a striking demonstration of the essential features of various types of cells in animal tissues. Schwann, moreover, recognized that the egg is a single cell, though he was unable to decide whether its nucleus (germinal vesicle) is indeed a nucleus or a young cell.

Both Schleiden and Schwann were inquisitive to know how new cells are formed. They knew as little about it as did Lamarck. Schleiden's guess, that a lens-shaped excrescence forms upon the surface of a nucleus and furnishes a sort of intracellular bud from which the new cell develops, has already been mentioned. Schwann thought that their germ is a nucleolus, which, escaping from the nucleus into an intercellular, cell-producing "cytoblastema," grows by a process akin to crystallization, first generating the new nucleus and then the surrounding protoplasm.

But to follow the cell theory further would bring us beyond its dawn and to the break of day, to the time when the question that had perplexed the mind of Schleiden, "How does this peculiar little organism, the cell, originate?", was answered by the discovery of the interesting phenomena presented by the nucleus in cell-division. That discovery brought the cell theory into a new epoch, fraught with new and perplexing questions as to the nature of the forces that divide nucleus and cytoplasm, and shape the growing organism.

As we ponder upon these problems and seek to devise new experiments to solve them, we should do well now and then to turn back to the suggestive thoughts of Lamarck, who, untrammeled by some of the modern working hypotheses that tend to become crystallized in our minds as dogma, approached the great problems of life with the keen mind of a seer.

Résumé: (1) The cell theory was stated originally by Mirbel and Lamarck in 1808 and 1809, thirty years before Schleiden and Schwann. (2) Mirbel, like Schleiden, showed in 1808 that all plants are composed of cells, of cellular tissue, which he regarded as everywhere continuous, primarily membranous, and variously modified into all other plant tissues. He laid especial emphasis in the earlier years of his brilliant investigations upon cell walls,

which he believed to be porous, allowing free, though slow, circulation of the contained fluids. (3) Lamarck, a year later, 1809, extended the idea of cellular origin to include both animal and plant structures. To him, cellular tissue was the matrix in which the organs (tubes of various sorts) are shaped by the movements of the contained fluids, which he regarded as essential vital substance. (4) Both Mirbel and Lamarck thought of the organism as a cellular whole, not as an agglomeration of units. (5) Dutrochet in 1824, adopting the Mirbel-Lamarck theory, introduced the idea of cellular units as composing the animal and plant organism, but the idea of the cell-unit had not yet been standardized and made definite by the discovery of the nucleus. (6) Robert Brown in 1833 recognized the universal occurrence of nuclei in all plant cells. The idea of the cell as a unit then became definite. (7) Schleiden in 1838 extended Brown's discovery by his own investigations of plant tissues, and stimulated his friends Schwann to research into the cell structure of animal tissues. He failed to discover how new cells originate, though this was the chief aim of his classic paper on phytogenesis. (8) Schwann in 1839 made a most important contribution to knowledge of animal histology, isolating, and accurately describing and drawing, many different varieties of cells. He added to the cell theory of Lamarck, Mirbel, and Dutrochet, guided by Brown's discovery of the nucleus, a clear-cut conception of the nature and limits of the individual animal cell. His elaborate speculative comparison between the origin and growth of crystals and of cells was founded on an erroneous belief as to the origin and development of new cells out of nucleoli, but, nevertheless, contains suggestions as to the nature of growth that foreshadow some of the more recent ideas of bio-chemistry and bio-physics.

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